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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,668	04/14/2006	Frank-Christophe Lintz	65177(45107)	1828

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EXAMINER	
HAGHIGHATIAN, MINA	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,668	LINTZ ET AL.	
	Examiner	Art Unit	
	Mina Haghighatian	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/03/09*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-41 and 44-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-41 and 44-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of the Remarks filed on 11/03/09. No claims have been amended, added or cancelled. Accordingly claims **25-41, 44-56** remain pending.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 25-26, 29-30, 35-41 and 44-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Malvolti et al (WO 03004005) in view of Nikolaizik et al (Bronchial constriction after nebulized tobramycin preparations and saline in patients with cystic fibrosis) and Hughes et al- The Lancet-2003 (Use of isotonic nebulised magnesium sulphate as an adjuvant to salbutamol in treatment of severe asthma in adults: randomized placebo-controlled trial) (Provided by Applicant in the IDS of 04/14/06).

Malvolti et al teach optimized formulations of tobramycin for aerosolization in the form of additive-free, **isotonic solution** whose pH has been optimized to ensure adequate shelf-life at room temperature. Said formulation can be advantageously used for treatment and prophylaxis of acute and chronic endobronchial infections (see abstract). In a preferred embodiment a formulation is prepared containing 300 mg of tobramycin sulfate in 4 ml of half-saline aqueous solution (0.45% of sodium chloride) in order to have an osmolarity ranging from **280** to 350 mOsm/l and it has a pH between 4.0 and 5.5 (page 5, line 25 to page 6, line 3). Other formulations have been prepared using **¼ normal saline** (see page 7). Malvolti et al disclose that the inventors of the patent EP 734249, it was discovered that "a further advantage of a **quarter normal saline**, i.e. saline containing 0.225% of sodium chloride with 60 mg/ml tobramycin is that this formulation is **more** efficiently nebulised by an ultrasonic nebuliser *compared* to tobramycin formulated in a solution of 0.9% normal saline (page 7, lines 11-15).

Malvolti et al also disclose a method of preparing the said formulations which includes the steps of adjusting the pH by adding an acid adjuvant such as sulfuric acid and also sterile filtering the solution (see pages 9-10). The prepared formulations are typically distributed in 2 ml polyethylene colorless unit dose vials under nitrogen purging (page 11, lines 11-12) and are administered by a nebulizer such as a PARI™ jet nebulizer (see page 14).

Tables 1 and 2 show a formulation that comprises between 67.5 and 82.5 mg/ml tobramycin.

Malvolti lacks disclosure on the addition of a magnesium or calcium salt. These deficiencies are cured by Nikolaizik et al and Hughes et al.

Nikolaizik et al teach that inhalation of commercially available preparations of tobramycin caused significant bronchial obstruction in CF patients with moderate to sever disease. It is also disclosed that placebo inhalations with isotonic saline caused similar large airway changes except for the complete cessation of peripheral air flows. Possible explanations could be an asthmatic reaction or the irritation of inhaled solutions inducing mucocilliary clearance (see page 610, under Discussion, first paragraph). Nikolaizik et al also discloses that salbutamol was able to prevent tobramycin–induced constriction.

Hughes et al disclose a trial that investigates the effect of isotonic magnesium administered as an adjunct to nebulized salbutamol. Magnesium is a powderful relaxant of smooth muscle in the airways (page 2114, 2nd paragraph). In a study, patients received 2.5 mg salbutamol mixed with 2.5 ml isotonic magnesium sulphate or isotonic saline (see Summary). It is then concluded that "Our results showed that use of isotonic nebulised magnesium sulphate as an adjuvant to salbutamol nebulizer solution results in an enhanced bronchodilator response in severs asthma. Administration of the salbutamol nebulizer solution with the magnesium adjuvant resulted in about twice the increase in FEV_1, than the same dose of salbutamol administered with an isotonic

saline nebulizer solution (page 2116, col. 2, 1st and last paragraphs and page 2117, col. 1, 4th paragraph).

Malvolti et al does not anticipate the claims because it does not disclose a formulation that contains 2 mg/ml sodium chloride or less, and does not teach addition of a magnesium or calcium salts. However it does disclose using ¼ normal saline and it is disclosed that lower concentrations of sodium chloride in the said solution formulation are beneficial. Nikolaizik et al also teaches that tobramycin and saline both caused broncho-constriction in CF patients. Thus one of ordinary skill in the art would have been able to optimize the concentration ranges of tobramycin and sodium chloride to prepare a more effective formulation. Furthermore, Hughes et al disclose that magnesium is a powerful relaxant of smooth muscle in the airway and that addition of magnesium sulphate is highly advantageous in treating asthma with salbutamol and that it enhances bronchodilator effect of salbutamol. Thus one of ordinary skill in the art would have been motivated to have combined the formulations of Malvolti et al and magnesium sulphate of Hughes et al in order to reduce the possibility of causing broncho-constriction or asthmatic effects in patients receiving tobramycin for their respiratory infections. In other words, **all the claimed elements** were known in the prior art and one skilled in the art could have **combined the elements** as claimed by known methods with no change in their respective functions, and **the combination would have yielded predictable results** to one of ordinary skill in the art at the time of the invention.

Furthermore, Malvolti lacks certain specifics of the claimed nebulizer or packaging such as closure elements and nose pieces, however it is considered while the said limitations are not expressly disclosed, they exist in the jet or ultrasonic nebulizers and packages disclosed by the prior art. It is also noted that the instant claims are drawn to "a sterile liquid preparation" and the packaging or mode of administration are not patentable elements of a formulation.

Claims 25-26, 29-30, 36-41 and 44-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Montgomery (6,083,922) in view of Nikolaizik et al (Bronchial constriction after nebulized tobramycin preparations and saline in patients with cystic fibrosis) and Hughes et al- The Lancet-2003 (Use of isotonic nebulised magnesium sulphate as an adjuvant to salbutamol in treatment of severe asthma in adults: randomized placebo-controlled trial) (Provided by Applicant in the IDS of 04/14/06).

Montgomery teach a method of treating chronic tuberculosis using a preservative-free concentrated tobramycin aerosol formulation delivering tobramycin to the lung endobronchial space (see abstract). The formulations for use in the said methods comprise from 40 to 800 mg of tobramycin in 5 ml of quarter normal saline. This corresponds to 8-160 mg/ml (col. 10, lines 9-17). The tobramycin formulations comprising 60 mg/ml of ¼ **NS** have an osmolarity in the range of 165-190 mOsm/l (col. 10, lines 52-55). The pH is between 5.5 and 7.0 (col. 10, lines 60-67).

Montgomery discloses that the formulations are administered by nebulizers such as jet and ultrasonic nebulizers. A jet nebulizer works by air pressure and an ultrasonic nebulizer works by piezoelectric crystal. Examples of the said nebulizers include Pari LC and Pari LC plus (see col. 12, lines 1-59). Examples 1-3 disclose the ingredients and amounts of the formulations. Other than tobramycin and saline, sulfuric acid is present. Montgomery also states that "Higher amounts of tobramycin was delivered when tobramycin was formulated in **¼ diluted saline** than tobramycin formulated in *full strength nondiluted saline"* (see col. 16, lines 17-19). The formulation is stored in polyethylene LDPE vials in foil overpouch (col. 16, lines 60-65).

Montgomery does not teach or suggest addition of a magnesium or calcium salt. These deficiencies are cured by Nikolaizik et al and Hughes et al.

Nikolaizik et al teach that inhalation of commercially available preparations of tobramycin caused significant bronchial obstruction in CF patients with moderate to sever disease. It is also disclosed that placebo inhalations with isotonic saline caused similar large airway changes except for the complete cessation of peripheral air flows. Possible explanations could be an asthmatic reaction or the irritation of inhaled solutions inducing mucocilliary clearance (see page 610, under Discussion, first paragraph). Nikolaizik et al also discloses that salbutamol was able to prevent tobramycin–induced constriction.

Hughes et al disclose a trial that investigates the effect of isotonic magnesium administered as an adjunct to nebulized salbutamol. Magnesium is a powderful relaxant of smooth muscle in the airways (page 2114, 2nd paragraph). In a study, patients received 2.5 mg salbutamol mixed with 2.5 ml isotonic magnesium sulphate or isotonic saline (see Summary). It is then concluded that "Our results showed that use of **isotonic nebulised magnesium sulphate** as an adjuvant to salbutamol nebulizer solution results in an enhanced bronchodilator response in severs asthma. Administration of the salbutamol nebulizer solution with the magnesium adjuvant resulted in about twice the increase in FEV_1, than the same dose of salbutamol administered with an isotonic saline nebulizer solution (page 2116, col. 2, 1st and last paragraphs and page 2117, col. 1, 4th paragraph).

Montgomery does not anticipate the claims because it does not disclose a formulation that contains 2 mg/ml sodium chloride or less, or the addition of a magnesium or calcium salt. However it does disclose using ¼ normal saline and that ¼ **normal saline is advantageous** because it allows for higher amounts of tobramycin being delivered, thus it would have been clear to one of ordinary skill in the art that lower concentrations of sodium chloride in the said solution formulation would be beneficial. One of ordinary skill would have been able to optimize the concentration ranges of tobramycin and sodium chloride to prepare a more effective formulation for aerosol administration. Furthermore, Nikolaizik et al teaches that tobramycin and saline both caused broncho-constriction in CF patients. Hughes et al disclose magnesium is a

powerful relaxant of smooth muscle in the airway and that addition of magnesium sulphate is highly advantageous in treating asthma with salbutamol and that it enhances bronchodilator effect of salbutamol. Thus one of ordinary skill in the art would have been motivated to have combined the formulations of Malvolti et al and magnesium sulphate of Hughes et al order to reduce the possibility of causing broncho-constriction or asthmatic effects in patients receiving tobramycin for their respiratory infections. In other words, **all the claimed elements** were known in the prior art and one skilled in the art could have **combined the elements** as claimed by known methods with no change in their respective functions, and **the combination would have yielded predictable results** to one of ordinary skill in the art at the time of the invention.

Claims 27-28 and 31-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Malvolti et al (WO 03004005) in view of Nikolaizik et al and Hughes et al as applied to claims 25-26, 29-30, 35-41, 44-56 above, and further in view of Wiedmann et al (5,747,001).

Malvolti et al, Nikolaizik et al and Hughes et al, discussed above lack specific disclosure on adding other isotonising agents and surface active adjuvants.

Wiedmann et al teaches an aerosol comprising droplets of an aqueous dispersion of nanoparticles, comprising an active agent having a surface modifier on the surface thereof (see abstract). The said modifiers include calcium stearate, magnesium aluminum silicate, lecithin (phosphatides), n-dodecyl ß-D-maltoside and tyloxapol (see

cols. 3-4). The said aerosols are typically administered by nebulizers such as jet and ultrasonic nebulizers (see col. 3, lines 17-28).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the formulations of the combined references by adding the surface modifiers/adjuvants as taught by Wiedmann et al with a reasonable expectations of successfully preparing formulations for inhalation that are stable and easy to flow. In other words, this rejection is based on the well established proposition of patent law that no invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive effect of the ingredients, In re Sussman, 1943 C.D. 518.

Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Malvolti et al (WO 03004005) in view of Nikolaizik et al and Hughes et al as applied to claims 25-26, 29-30, 35-41, 44-56 above, and further in view of Azria et al (5,759,565).

Malvalti et al, Nikolaizik et al and Hughes et al, discussed above, lack specific disclosure on viscosity of the formulations.

Azria et al teach pharmaceutical compositions for nasal administration, comprising an active and a surfactant in a liquid carrier. The said compositions should

possess appropriate isotonicity and viscosity. The preferred osmotic pressure is from about 260 to about 380 mOsm and the viscosity is from about 2 to about $4x10^{-3}$ Pa.S (see col. 4, lines 5-30).

It would have been obvious to one of ordinary skill in the art at the time the invention was made given the general formulations of the combined references on nebulizer solution formulations comprising an active agent and surfactants to have looked in the art for suitable and appropriate isotonicity and viscosity for the formulations as taught by Azria to prepare and effectively deliver a solution formulation to the mucosa for maximum absorption and systemic distribution.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant's arguments filed on 11/03/09 have been fully considered but they are not persuasive.

Applicant has traversed all rejections and submitted two documents in support of their arguments. Applicants arguments and in view of the submitted documents have been fully considered and found not persuasive.

Applicant states that arts such as Nikolaizik, report bronchoconstriction occurs upon tobramycin inhalation, however, "it is unclear if the observed bronchoconstriction is released to certain formulation excipients, particularly sodium metabisulphate and phenol". This is not persuasive because Nikolaizik discloses "...antioxidants and preservatives which **also** cause bronchial obstruction". Thus the use of the term "also" is interpreted as Nikolaizik disclosing that tobramycin causes bronchial obstruction and that excipients may also cause it. This is not a teaching away.

Applicant argues that in a study done by Alothman et al, it was concluded that "...preservative-containing IV preparation caused more bronchospasm in LR group than preservative-free solution". Then Applicant argues that "this confirms the suggestion of Nikolaizik that the bronchoconstriction was most likely a result of preservatives rather than tobramycin". This is not persuasive because the conclusion was that "preservative-containing IV preparation caused **more** bronchospasm...". Again, the disclosure is interpreted as stating that preservatives may add to the bronchoconstriction, not that they are the sole cause. In fact this is a confirmation that tobramycin by itself causes bronchoconstriction.

Applicant then concludes that given the teachings of Alothman et al and Nikolaizik et al, one would not be motivated to add magnesium to the tobramycin formulations. This is not found persuasive because as shown in the rejection, the combination of references teach one of skilled in the art to add magnesium to prevent or lessen the bronchoconstriction effects of tobramycin. Furthermore, as shown above, the teachings of Alothman et al and Nikolaizik et al do not teach that it is the excipients that

cause the bronchoconstriction, but that some excipients may add to the effect. Hughes et al clearly discloses that magnesium is a powerful relaxant of smooth muscle in the airways, and that isotonic magnesium is a beneficial adjuvant to nebulized salbutamol which results in an enhanced bronchodilator response in treatment of asthma. Thus there is sufficient motivation for one of ordinary skill in the art to have added magnesium to the tobramycin formulations with an expectation of successful bronchodilation and treatment of asthma.

Applicant also argues that "according to Hughes, a concentration of 250 mmol/L, resulting in an isotonic solution with osmolality of 289 mOsmol was used. However, as Mg sulphate is expected to dissociate in two ions when dissolved in water, the calculated osmolality should be approximately 500 mOsmol/L. It is not clear from publication why osmolality mentioned by Hughes is much lower" (see page 10 of response). Applicant continues that "Taking into consideration that the reported results of inhaled magnesium are already uncertain, a skilled person will not have a reasonable expectation of success by reducing the magnesium concentration to the above calculated concentrations, far below what is indicated in the prior art. According to calculations starting from the instantly claimed tobramycin concentration, it becomes clear that the magnesium concentrations that can be applied in the claimed tobramycin formulations can never be as high as in the studies where inhaled magnesium has been studied" (see page 11).

The above arguments are not persuasive. Firstly, both Malvolti and Hughes et al teach one of ordinary skill in the art that the suitable osmolality for inhalation of active

agents to the lung is between 250-450 and preferably from 280-350 mOsmol/L. One of ordinary skill in the art having possession of this teaching and the specifics of tobramycin and magnesium salts can easily adjust to obtain the desired osmolality. Secondly, Malvolti et al, the primary reference is relied upon for its teachings of the osmolality and Hughes was relied upon for its teachings of addition of isotonic magnesium salts, for its bronchodilation effects. Thirdly, Hughes et al discloses that the formulation is isotonic. Forthly, claims do not recite any specific amount of magnesium salt.

Additionally, it is noted that Hughes et al reference **IS** the reference Applicants have relied upon for addition of calcium or magnesium salts, their effect on bronchodilation and their determination of isotonicity (see Spec, page 6, lines 30-35).

With regards to Applicants argument that "reported results of inhaled magnesium are already uncertain", Examiner disagrees with this statement, because as argued above, it has clearly been established by the prior art that inhaled magnesium is a suitable adjuvants, a powerful muscle relaxant in the airways and that it results in a significantly greater improvement of FEV (see Hughes, pages 2114, 1st and 2nd col, and page 2116, last paragraph under discussion).

Applicant then argues that "Around the date of the filing of the instant application, the effects of inhaled magnesium sulphate were still not known as demonstrated by Aggarwal et al. (Emerg. Med. J. 2006.23:258-362, copy enclosed)" (See Response, page 11). This is not persuasive. In fact Hughes et al reference which was published in June 2003 is relied upon in the instant Application. Thus it was well established at the

time of instant invention that magnesium sulphate is a suitable adjuvant and a powerful bronchodilator.

Applicant argues that "The Office Action notes that Malvolti does not suggest the use of magnesium or calcium in the formulation, and relies upon Nikolaizik et al. and Hughes et al. to overcome this deficiency. However, there can be no motivation to increase the osmolality of the formulations of Malvolti, having optimized administration of tobramycin by reducing the osmolality, particularly to isotonic magnesium as suggested by Hughes" (see Response, page 12). This is not found persuasive because Malvolti teaches that suitable osmolality for inhalation of formulations to the lung is preferably from 280-350 mOsm/L. Hughes teaches that the formulations should have a osmolality of about 289 (which lies in the preferred range as taught by Malvaolti). Thus one of ordinary skill in the art is not required to increase the osmolality of the formulations of Malvolti, but to adjust when the magnesium salt is added to make sure that the total osmolality of the formulation is in the desired range.

Furthermore, according to MPEP 2144.05: "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969); Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10

USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed.Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

The next argument is that "The effect of Hughes observed with administration of salbutamol with severe asthma cannot provide motivation to add magnesium to tobramycin for nebulized administration. Salbutamol is a rapid-acting, short-acting 132-adrenergic receptor agonist used for the relief of bronchospasm in conditions such as asthma and chronic obstructive pulmonary disease. Tobramycin sulfate is an aminoglycoside antibiotic used to treat various types of bacterial infections, particularly Gram-negative infections. There is essentially no commonality in the mechanism of actions of the drugs, the subjects to be treated using the drugs, or the events to prompt treatment with the drugs" (see Response, page 13).

This is not persuasive either because while the two drugs are different with different mechanism of action, the combined references would provide one of ordinary skill in the art with sufficient teachings and motivation to add magnesium salts to tobramycin formulations as well. Malvolti et al teach tobramycin formulations for inhalation. Nikolaizik et al teach that nebulized tobramycin preparations cause bronchial constriction and Hughes et al teach that adding isotonic magnesium salts are suitable adjuvants to relieve bronchoconstriction caused by medicaments such as salbutamol. It is disclosed that magnesium is a powerful smooth muscle relaxant in airways. Applicant has not shown why one of ordinary skill in the art would not be motivated to add isotonic magnesium salts to tobramycin formulations to prevent them from causing

bronchconstriction in patients. In other words, the claims would have been obvious because a person of ordinary skill has good reasons to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

Furthermore, a reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976).

Conclusion

Claims **25-41, 44-56** remain rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is (571)272-0615. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mina Haghighatian/

Mina Haghighatian
Primary Examiner
Art Unit 1616